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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/106,390 06/26/98 THOMSON J 96-0296-9540

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EXAMINER

CLARK, D

ART UNIT

PAPER NUMBER

1633

DATE MAILED:

09/24/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/106,390

Applicant
Thomson, James A.

Examiner
Deborah Clark

Group Art Unit
1633



- ☐ Responsive to communication(s) filed on _____
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-11 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-11 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claims _____ are subject to restriction or election requirement.

Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of References Cited, PTO-892 ✓
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5 ✓
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948 ✓
- ☐ Notice of Informal Patent Application, PTO-152
- x Notice to Comply ✓

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-8 are directed to a purified preparation of human embryonic stem cells. Claims 9 and 10 are directed to a method of isolating a human embryonic stem cell line. Claim 11 is directed to a cell line developed by the method of claim 9.

The specification does not enable one of skill in the art to practice the claimed invention. The nature of the claimed invention is human embryonic stem (ES) cells. By definition, embryonic stem cells are able to contribute to all tissues of an animal including the germ cells (see Nichols et al., page 1341, ¶ 1). The state of the art of the claimed invention is not well established, very few species of animal has had true ES cells isolated. As admitted by applicants only rodent ES cells have been fully characterized (see page 7 of the specification). The art of isolating ES cells is highly unpredictable. Cruz et al. list some of the differences in early embryonic development among swine, oxen, horses, goats, and sheep (see Table 1, page 166).

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Piedrahita et al. observed that porcine and ovine embryos responded differently to the same treatments. Conditions that allowed production of porcine ES-like cell lines did not allow development of ovine ES-like cell lines (see Table 1, page 886, and page 888). Therefore, one cannot extrapolate from procedures shown effective in one species to another species. As demonstrated by the art cited above numerous attempts have been made to isolate ES cells from species other than the mouse, but (other than the porcine ES cells as claimed by Wheeler (copy enclosed)) demonstration that these cells are able to contribute to the germ line is awaited (see Clark et al., page 250, ¶2). The guidance set forth in the specification is not sufficient to enable one of skill in the art to isolate human cell lines. The specification sets forth a procedure for the isolation of primate ES cells. However, this procedure has been shown as successful only as far as the demonstration of certain markers, expression of chorionic gonadotropin, and differentiation into cells representative of each of the three layers of the embryonic germ layers when injected into SCID mice for two species, rhesus macaques and marmosets. No data is set forth regarding humans, which is specifically claimed. And, no data demonstrates that the rhesus or marmoset "ES cells" can contribute to the germline. The amount of experimentation required to practice the claimed invention is paramount. It is not clear that the procedure used in the monkey species would be successful in the human species. In addition, the amount of experimentation required to demonstrate that ES-like cells are true ES cells is vast because the ES-like cells would need to be implanted into a blastocyst, allowed to grow to term, and then demonstrated to have true mosaicism in all tissues including germ line cells.

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Therefore, given the nature of the claimed invention, the state of the art, the level of predictability found in the art, the guidance set forth in the specification, the working examples set forth in the specification, and the amount of experimentation required to practice the invention would require undue experimentation on the part of the skilled artisan.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "capable of" in regard to proliferation. This recitation renders the claim unclear because how is one to determine what the cell is "capable of" unless actually demonstrated. The claim should be amended to recite that the cell does proliferate.

Claims 1 and 3 recite "chromosomes characteristic of the human species". This recitation renders the claims indefinite. In what way is a chromosome "characteristic" of the human species? The skilled artisan is not reasonably apprised as to the scope of the claims. The examiner notes that the specification states that the ES cells are euploid. Such a recitation would be clear and definite.

Claims 1 and 3 recite that the chromosomes are "not noticeably altered" or that "none of the chromosomes are noticeably altered", respectively. This recitation is indefinite because there

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is no requisite degree in which to base the alteration. Therefore, the skilled artisan is not reasonably apprised as to the scope of the claims.

Claim 3 recites that the cells are “essentially” negative or positive for certain markers. This recitation makes the claims indefinite because there is no requisite degree with which to base the level of markers that is considered negative or positive. Deletion of the word “essentially” is recommended.

Claim 9 is indefinite because the steps of the method do not necessarily lead to the claimed invention. The claimed method is incomplete. Following the steps of claim 9 does not necessarily lead to the claimed method because the steps of the invention do not require that the cells are actually cultured beyond a primary culture or that the cells are true ES cells. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter the claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6. The claim should be amended to recite that a human ES cell line is obtained.

Claim 11 recites “a cell line developed by the method of step 9”. This recitation is indefinite because there is no step 9. It is presumed that applicants intended to say of claim 9. Correction is required.

Claims not specifically addressed above are rejected due to their dependency upon either of claims 1, 3, or 9.

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Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-11 are rejected under the judicially created doctrine of double patenting over claims 1-11 of U. S. Patent No. 5,843,780 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the patent, '780 claims primate embryonic stem cells. The instant application claims human embryonic stem cells. A human is a primate. Therefore, the claims directed to human ES cells would extend an embodiment of the claims of '780.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968).

See also MPEP § 804.



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Sequence Rules

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). A computer readable form (CRF) of the sequence listing was submitted. However, the CRF could not be processed by the Scientific and Technical Information Center (STIC) for the reason(s) set forth on the attached CRF Diskette Problem Report.

Applicant is must comply with the sequence rules, 37 CFR 1.821 - 1.825 in response to this office action. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached CRF Diskette Problem Report with the reply.

Conclusion

8. No claim is allowed.
9. The examiner is aware that applicants have undertaken experiments with human cells post filing (see Thomson et al., enclosed). It is recommended that applicants make this data of record by way of a declaration filed under 37 CFR 1.132.
10. Claims 1-11 are free of the prior art of record. Claims 9-10 are directed to methods of isolating a cell line and claim 11 is directed to a cell line. The prior art does not disclose any human ES or ES-like cells which were maintained as a cell line. Claims 1-8 are directed to a

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purified preparation. The closest prior art which can be represented by Bongso et al., as presented by applicants, demonstrates isolation of human embryonic cells from the inner cell mass. However, the isolated cells were not fully characterized. The cells did have stem-cell like morphology, expressed alkaline phosphatase, and had a normal karyotype, however, it was not reported that the cells would contribute to the germ-line, the cell markers were not set forth, whether they expressed chorionic gonadotropin or telomerase, and it was only shown that they would differentiate into fibroblasts. Therefore, the cells cannot be considered true ES cells and therefore do not anticipate or obviate the claimed invention.

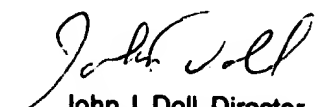
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Clark whose telephone number is (703) 305-4051. The examiner can normally be reached on Mondays-Fridays from 7:10 a.m. EST to 3:40 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Stanton, can be reached on (703) 308-2801. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

10. The signature of the group director indicates his concurrence with the rejections.


DEBORAH J. CLARK
PATENT EXAMINER


John J. Doll, Director
Technology Center 1600